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The Pathomechanical Etiology of Ankle Post Traumatic Osteoarthritis

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It is commonly noted that the prevalence of osteoarthritis in ankle joint secondary to a traumatic event is relatively high. Approaches to limit such occurrences are often directed by the perceived need of anatomical reduction. However the progression to osteoarthritis is often observed irrespective of the degree of osseous relocation. The premise therefore is that pathomechanical etiology of post traumatic osteoarthritis in the ankle is poorly understood. Beyond articular joint incongruities, both direct initial articular insult and instability are believed to play a role. This review will therefore explore and evaluate the significance of these potential mechanical causalities in an attempt to clarify the etiology of traumatic ankle osteoarthritis.

Key words: Post traumatic osteoarthritis, Cartilage, Ankle joint incongruity, Ankle joint instability

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The prevalence of osteoarthritis (OA) in adults ≥ 45 years of age in the knee and hip occurs at a rate of 27.8% and 27% respectively, this is significantly higher compared to the reported occurrence of OA in the ankle joint (4.4%) [1, 2]. When ankle arthritis does occur however it is commonly observed after a traumatic event. Indeed Saltzman's study towards the epidemiology of ankle arthritis showed that 54% of all ankle arthritis were secondary to trauma [3]. This is significant when considering that in the same scenario a rate of 9.8% and 1.6% in the hip and knee has been reported respectively [4]. Marsh has also stated that 30% of ankles develop radiographic evidence of OA within 2-4 years following a tibial plafond fracture, and 74% in 5-11 years [5, 6].

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As the rate of ankle OA remain low in a non-post-traumatic joint, we are therefore obligated to conclude that changes to the joint via injury operate as the instigating factor for future OA. The question then arises as how such an event predisposes an otherwise arthritic impervious joint to display high levels of arthritis. Despite knowledge of its cause of occurrence, the true pathomechanical etiology remains poorly understood. This is perhaps largely due to an inability to observe exclusively and quantify the effects of direct trauma, incongruency and instability to ascertain their significance towards ankle PTOA. This review will explore the current understandings and beliefs as to the etiology behind ankle PTOA in an attempt to gain clarity towards the significance of such mechanical variables.

Articular Trauma

Many have simply argued that the occurrence of PTOA is

the result of the direct traumatic compromise to the articular surface. Indeed Lindsjo suggested that rate of PTOA correlated to the degree of articular insult at the time of injury. He found that the degree of arthritis was greater with ankle fractures involving large articulating posterior maleolar fractures regardless of the extent of anatomical reduction [7]. If one is permitted to assume that ankle fracture severity correlates with cartilaginous insult, then credence is also provided by the work of Horisberger in his long-term retrospective cohort study [4]. Horisberger observed that not only did fracture severity influence the rate of development of OA but also the latency time to end-stage OA (decreased latency with increased severity). Additional support is also partly provided by Marsh's 2003 study of tibial plafond fractures in which it can be acknowledged that the greatest degree of injury correlated to the higher levels of arthrosis (at 5 year f/u) [6]. In vivo studies by Haut has also shown development of surface fissures via impact on rabbit patellofemoral joints resulting in measurable degrees of cartilage softening for which it is argued provides the mechanism of development of PTOA [8]. With such validation, it is encouraging to conclude that the severity of articular injury is the primary determinant of future OA. However, reluctance towards such a stance is based on the apparent inability to truly measure injury severity (beyond in vivo animal studies); indeed the common-place practice of using fracture classifications towards this endeavor remain rudimentary and plighted by poor intra-observer reliability [9]. Thus without an ability to quantify severity, conclusions towards its significance in ankle PTOA remain speculative. This was the argument offered by Anderson in his exceptional work on the pathomechanical etiology of PTOA in which not only was this limitation highlighted, it was addressed [10]. Anderson 'ab initio' approach argued that severity of injury is equal to the energy released during fracture, this energy released can be quantified based on measuring the created inter-fragmentary surface area (*via* CT). Despite significant variations in fracture patterns, the surface area measurements showed strong correlation to applied energy in model studies. When applied to clinical studies, it was found that fracture energy and articular comminution was able explain 70% of PTOA severity (based on Kellgren-Lawrence grading). In addition, the data suggested the existence of a severity threshold, below which OA was not observed. One can perhaps conclude therefore that articular insult severity plays a considerable role towards the generation of PTOA. However, given the quoted percentile it remains incomplete and limited as singular comprehensive tool in PTOA prediction. This observed deficit might be explained in the current omission to discuss congruency and the perceived necessity of accurate reduction.

Congruency

Seemingly contrary to his initial findings, Lindsjo in his 1985 paper went on to anecdotally observe that the frequency of PTOA was lower with those ankle fractures that were reduced under AO approach [7]. Indeed, Horisberger speculated that his observed prolonged latency period (from initial ankle trauma to end-stage OA) could be attributed to improved reduction techniques [4]. Reudi also observed favorable functional results with anatomical reconstructions compared to conservative treatment for pilon fractures in his 9-year follow up study [11]. It has thus generally been thought that the degree of similarity towards that of anatomic relocation is paramount in the attempt to reduce the likelihood of ankle PTOA. Such a stance however remains hindered by a lack of supportive comprehensive data, which has limited the association of degree of incongruency to severity of PTOA [5].

The true complexity of the effect of incongruency on PTOA begins to reveal itself when we consider the work of Giannoudis and his literature review exploring the effect of articular step off and the risk of PTOA in various joints [12]. Giannoudis highlighted the fact that different joints respond differently to intra-articular injuries of comparable magnitude; such notion is followed by the observation that the ability to reduce PTOA *via* accurate reduction is subject to the joint in question. For example reduction of the superior articular surface of the acetabulum has shown strong positive correlation towards clinical and radiographic outcomes. This is contrasted when one considers the lateral tibia plateau fractures in which the quantity of articular congruency has been reported to be independent of outcome [13, 14]. Speculations as to the cause of such disparities were attempted by Llinas who suggested that mechanisms towards restoring articular congruency are indicative of the size of the step-off relative to the thickness of the articular cartilage [15]. He noted that improved pressure differential across the articular surface for a step-off not exceeding the cartilage thickness after 12 weeks in rabbit medial femoral condyles.

This was further supported by Trumble, who found increased matrix material and chondrocyte hypertrophy on the low side compared to collagen compression on the high-side of a created 1mm step off of the tibial plateau in adult sheep [16]. Given that the average cartilage thickness of such specimen's were 1.5mm it is argued that articular fractures show better remodeling when contact between adjacent articular cartilage remain. To clarify, it is thus postulated that sensitivity of step-off is inversely proportional to cartilage thickness. Such notions are seemingly supported when one considers that the average cartilage thickness for the acetabulum and tibial plateau are 1.15mm and 2.92 respectively [17, 18].

The theory would appear to also extend to the articular cartilage of ankle; Shepherd and Seedhom looked at the articular cartilage of the hip, knee and ankle in 11 cadaveric specimens noting significant differences in thickness for each anatomical group [17]. The ankle displayed the thinnest of cartilage (1.0 to 1.62mm), significantly ($p< 0.001$) lower than that observed for the hip (1.35 to 2.0mm) and knee (1.65 to 2.55mm). Shepherd also found an inverse relationship between thickness of articular cartilage and its compressive modulus thus presumably preserving ankles ability to maintain congruency. Indeed, Simon et al postulated that the thickness of cartilage was inversely correlated to a congruence ratio, such that joints that required congruency have thinner cartilage with little deformity [19]. The thickness of the articular cartilage of the ankle thus provides us with a paradox; its minimal nature perhaps provides resilience to incongruency, however when incongruency does occur (i.e. when the level of resilience is exceeded), its ability to respond to such deformity is limited. Despite these apparent complexities, such notions would indeed support the initial observations of Lindsjo. Furthermore, the concept of a level of resilience supports Anderson's observations of a severity threshold. If one therefore adheres to such conclusions, then the necessity to accurately quantify the degree of incongruency becomes apparent. To this regard the sensitivity towards step-off in ankle fractures is observed in the work of Drijfhout van Hoof in his study towards the long-term outcome of posterior malleolar fractures [20]. Drijfhout found that a step-off of >1mm resulted in significant higher rate of OA (radiographically) regardless of fixation protocol in a mean 6.9 year follow-up. Langenhuijsen also concluded that reduction of posterior malleolar fractures (>10% of articular surface) that obtained congruency (<1mm step off) faired better based on radiographic and clinical scores compared to their incongruent counterparts [21]. Such studies are of course limited to incongruencies associated with step-off type morphology created by the reduction of relatively simple intra-articular fractures. The ability of post-reduction radiographs (as is often the approach) to accurately measure articular surface incongruity associated with more morphologically complex fractures (i.e. pilon) is however poor (presumably due to the inability to appreciate subtle changes in such minimal cartilage) [22]. Hence the degree to which injured articular joints tolerate elevated contact stress is unknown and thus so is the required level of articular reduction. Such predicament was highlighted by Anderson's work on contact stress elevations via finite element (FE) stress analysis, a computed modality able to measure discrete changes in congruency [23]. It was found that larger percentages of post-fracture cartilage experienced high contact stress compared to their intact ankle counterparts. Additionally, 100% prediction accuracy for OA was associated with a critical stress-time-dose of 3MPa-s/gait cycle. The study again suggests a threshold concept, in this case contact stress exposure, above which PTOA is likely.

Instability

This advocacy towards the necessity of adequate reduction in order to reduce the rate of PTOA can be considered the current mainstay approach among surgeons to date. Others however have considered that the level of stability may be a more significant determinate of PTOA. This has perhaps been most notably highlighted in Rasmussen's study of tibial plateau fractures, in which 87% of patients had good outcomes regardless of articular surface reduction provided that coronal plane stability was maintained [24]. When one considers the ankle joint, we are compelled to consider the observations of Harrington who noted progressive arthritic degeneration of the talus and tibial plafond with chronic lateral ankle instability in the absence of acute cartilaginous trauma [25]. Indeed, Valderrabano, in his study noted 13% of all ankle arthritis was the result of ligamentous lesions predisposing the patient to ankle instability [26]. However, despite speculations that progressive cartilaginous degeneration is therefore the result of instability derived pathological forces at the ankle mortise, one must also consider (as noted by Valderrabano) the degree of cartilage damage at

the time of injury that is invariably reviewed in such studies and should not be assumed to be negligible. Moreover, in the objective of exploring the influence of chronic focal abnormal ankle joint stress towards the generation of PTOA, it becomes prudent to attempt to distinguish and decipher the stress generated via instability compared to that of incongruency. This was indeed attempted by McKinley in his 2008 study on the effect of incongruency and instability in human cadaveric ankles [27]. Contact stress directional gradients were measured in cadaveric specimens with an anterior 1/3 distal tibia 2.0 mm step off (to create incongruity) and severed anterior talofibular ligament (to create instability). By rotating the ankle through the stance-phase ROM, stresses were measured with a 300N axial load and with an application of an anterior to posterior pulse to cause subluxation. It was found that transient contact stress directional gradients increased by 60% at the subluxation event compared to stable incongruous conditions. Given the premise that increased stress gradients can lead to cartilage degeneration it is speculated that instability can have a significant influence on PTOA [28]. McKinley's study therefore supports the assertion that early stabilization is required in the reduction of development of degenerative arthritis. Although this may indeed be the case, one needs to be cognizant of the fact the value of instability is measured in presence of incongruity and as such it does not provide an appreciative handle on its sole influence on PTOA generation.

Conclusion

We have seen that direct trauma, incongruency and instability can all play a role in the generation of PTOA. The challenge arises when attempts are made to isolate the effects of each mechanical determinant to evaluate their significance. To obtain significance one needs to be able to quantify each effect, which has been largely restricted to *in vitro* and computational studies. We must also question whether one can truly isolate such effects in *in vivo* human studies. For example if minimal residual joint incongruencies are deemed to have an effect on the progression of PTOA then initial cartilaginous trauma can not occur without the acquiring articular inconsistencies. Furthermore an incongruous joint is likely to have additional elements of instability and vice versa, indeed McKinley noted that since unstable motion can arise from joint incongruity both pathomechanical entities could coexist [27]. In addition our discussion on acute impact does not encompass the progressive nature of such scenarios and their long-term biological connotations. Indeed, it has been argued that initial cartilaginous injury is merely the catalyst required for a cartilage degradation cascade [29]. This is perhaps likely considering the delayed presentation of OA and if one chooses to exclude the chronic effects of incongruency and instability. Borrelli et al used an open joint model to investigate the impact load effects on chondrocytes [30]. It was found that higher impact loads (500N) resulted in significantly higher levels of chondrocyte apoptosis compared to the lower impact group (400N). As chondrocytes are responsible for maintaining the integrity of articular cartilage by responding to mechanical stress it is speculated that such cell death is a significant contributor to the development of PTOA. More recently, Adams et al has investigated the hypothesis that the early inflammatory response within the synovial environment after intra-articular injury could lead PTOA [31]. Adams demonstrated that a pro-inflammatory, ECM degenerative environment was generated after intra-articular ankle fractures similar to which is seen in idiopathic OA. However, such investigations, as stated excludes the deleterious long-term effects of incongruency and instability. Arguably both factors can generate OA without initial discernable cartilaginous injury. The question therefore is whether such chronic scenarios can generate the same biological event as a significant initial cartilage injury. Indeed Borelli study found chondrocyte apoptosis occurred without fracture, which perhaps would therefore allow one to incorporate incongruency and instability within the theory [30]. It is thus somewhat desirable to conclude that generation of ankle PTOA is by biological cascade of events generated by direct impact and/or the repetitive abnormal insult on the ankle joint generated by the resultant incongruency or instability. If this statement is assumed then perhaps endeavors to isolate and evaluate the pathomechanical determinates of PTOA become inconsequential and in any case extremely challenging. Furthermore it was also suggest that further work towards the cause and treatment of PTOA should be directed towards the biological pathway as a consequence of the mechanical stress.

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